Effectiveness of a Strategy to Improve Adherence to Tuberculosis Treatment in a Resource-Poor Setting

A Cluster Randomized Controlled Trial

Sylla Thiam, MD
Andrea M. LeFevre, PhD
Fatoumata Hane, MSc
Alimatou Ndiaye, MD
Fatoumata Ba, DPharm
Katherine L. Fielding, MSc, PhD
Moustapha Ndir, MD
Christian Lienhardt, MD, MSc, PhD

Context Poor adherence to treatment remains a major obstacle to efficient tuberculosis (TB) control in developing countries. Innovative strategies to improve access and adherence to treatment are needed.

Objectives To assess the effectiveness of a contextualized intervention strategy aimed at improving patients' adherence to treatment and to evaluate its impact on TB control in a resource-poor country in Africa with prevalent TB infection.

Design, Setting, and Patients A cluster randomized controlled trial, conducted between June 2003 and January 2005, at 16 government district health centers in Senegal. Patients older than 15 years with newly diagnosed sputum smear–positive pulmonary TB were randomly assigned to the intervention or control group.

Intervention The intervention strategy included reinforced counseling through improved communication between health personnel and patients, decentralization of treatment, choice of directly observed therapy (DOT) supporter by the patient, and reinforcement of supervision activities. In the control group, the usual TB control program procedures remained unchanged.

Main Outcome Measure Proportion of patients successfully completing the 8-month course of treatment and the proportion of patients defaulting from treatment.

Results A total of 1522 patients were recruited into the study. Treatment was successful for 682 (88%) of 778 patients recruited in the intervention group, and for 563 (76%) of 744 patients recruited in the control group (adjusted risk ratio [RR], 1.18; 95% confidence interval [CI], 1.03-1.34). The proportion of patients defaulting was reduced in the intervention group to 5.5% (n=43) compared with 16.8% (n=125) in the control group (adjusted RR, 0.43; 95% CI, 0.21-0.89).

Conclusion The intervention package based on improved patients counseling and communication, decentralization of treatment, patient choice of DOT supporter, and reinforcement of supervision activities led to improvement in patient outcomes compared with the usual TB control procedures. This approach may be generalized in the context of TB control programs in resource-poor countries.

Trial Registration clinicaltrials.gov Identifier: NCT00412009

JAMA. 2007;297:380-386 www.jama.com

POOR ADHERENCE TO TREATMENT remains a major obstacle in the global fight against tuberculosis (TB).[1] Reasons for nonadherence are complex and multifaceted involving more than the patients' personal characteristics and attitudes.[2] Factors, such as the chronic nature of the disease, the socio-cultural context and poverty, and interacting with physicians, nurses, and other health care workers, all affect access to and adherence to treatment.[3-5]

In the World Health Organization (WHO) Africa region, 11% of the new smear-positive pulmonary TB cases diagnosed in 2002 were reported to have defaulted from treatment.[6] In Senegal, reported cure rates in the years before our study were low (53% on average between 2000 and 2002) with a high proportion of patients interrupting treatment before completion (28% on average during the same period).[7]

To address the problem of low adherence and improve treatment outcomes in Senegal, we undertook an interdisciplinary project that combined a qualitative study investigating the determinants of cure and a quantitative assessment of outcomes with the view to develop and test a novel and sustainable strategy.[8] The main identified impediments to successful patient outcomes were difficulties accessing treatment, poor communication between health care personnel and patients,

Author Affiliations: Institut de Recherche pour le Développement (IRD), Programme Tuberculose, Dakar, Senegal (Drs Thiam, Ndiaye, and Lienhardt, and Ms Hane); Infectious Disease Epidemiology Unit, London School of Hygiene and Tropical Medicine, London, England (Drs LeFevre and Fielding); Programme National de Lutte anti-Tuberculeuse, Dakar, Senegal (Drs Ba and Ndir); and International Union Against Tuberculosis and Lung Diseases, Paris, France (Dr Lienhardt).
Corresponding Author: Christian Lienhardt, MD, MSc, PhD, IRD and International Union Against Tuberculosis and Lung Diseases, 68 Blvd St Michel, Paris, 75006 France (clienhardt@iuatld.org).

poorly applied directly observed therapy (DOT), lack of a strategy to search for defaulting patients, and limited supervision of the treatment units by the district leadership team.[9] To assess the feasibility and effectiveness of the strategy developed on the basis of these findings and evaluate its potential impact on TB control, we undertook a cluster randomized controlled trial (RCT), which we report herein.

METHODS

Study Design

Senegal is a West African country, with a population of approximately 10 million. Health services are provided nationwide through 53 district health centers (DHCs). Tuberculosis diagnosis and treatment are integrated into basic health services and undertaken within TB control units in the DHCs, usually staffed with a nurse and health care assistants. Treatment is free and consists of a standard 8-month regimen (2 months intensive phase of combined rifampicin, isoniazid, pyrazinamide, and ethambutol, followed by 6 months continuation phase of combined isoniazid and ethambutol). Drug provision and patient monitoring are the responsibility of the National TB Control Program (NTCP).[7]

The cluster RCT design was chosen because the intervention was implemented at the health center level. The DHC was therefore the unit of randomization. The purpose of the intervention was to improve access to care and increase adherence to treatment, simultaneously targeting DHC staff, patients with TB, and communities, and included 4 components: (1) improving counseling and communication between health personnel and patients through appropriate training; (2) decentralizing treatment to remote health posts and involving community health workers; (3) strengthening the DOT strategy by giving patients the opportunity to choose their treatment supporter; and (4) reinforcing supervision of health posts by the DHC team.

Training of health care personnel was conducted over 4 sessions. The first session, conducted before the study commenced in both trial groups, reviewed the general principles of TB control, as outlined in the NTCP manual, to standardize knowledge at baseline. Subsequently, 3 training sessions (2 before recruitment and another 6 months after the study started) were run for the TB control staff working at the DHCs and health posts (nurses, assistant nurses, and community health workers) in the intervention group only. The objectives were to teach the health personnel about how to improve relationships with patients with TB, acquire negotiation skills, and provide appropriate counseling on TB and its treatment.

In each intervention DHC, treatment was commenced under direct supervision by the TB nurse, who then referred the patient to the health post nearest to his/her home for treatment delivery and follow-up by the health post nurse. At the health post, the health post nurse provided further information to the patients and asked each patient to identify a "DOT supporter" from his/her immediate surroundings. This supporter had to directly observe the daily drug intake and received training about all aspects of the treatment process. During the intensive treatment phase, anti-TB medication was to be collected by the DOT supporter on a weekly basis from the health post. During the continuation phase, the medication was delivered to the DOT supporter every fortnight. In case of adverse events, the patient was referred to the DHC. Patients who were in danger of stopping treatment before completion were systematically visited by the community health worker and encouraged to adhere to TB treatment. Lastly, the DHC leadership provided supervision and reinforced all aspects covered by the training to the health post staff when anti-TB drugs were supplied to the health post.

Patients recruited into the control group received the usual NTCP care,[7] being diagnosed, treated, and followed up in the TB control unit by the nurse as usual practice in each DHC. There was no specific community involvement, no decentralized treatment, no choice of DOT supporter, and no strategy to search for defaulting patients.

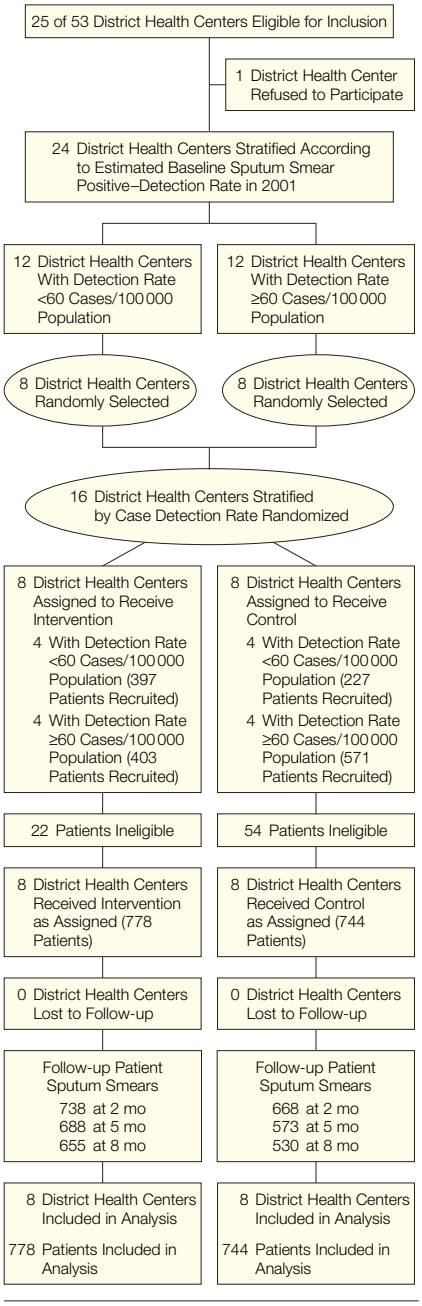
DHCs and Sample Size

Based on the detection of an average of 100 new TB cases per DHC per year, we calculated the required sample size aiming to detect a difference of at least 15% in the treatment success rate between the intervention and control groups. We assumed a coefficient of variability k=0.12 among DHCs, based on the success rates from all districts using conventional NTCP procedures in Senegal at baseline, and estimated that the success rate in the control group would be 65%. With 80% power, and a type I error of 5%, we calculated that 8 DHCs were required per group.[10]

District health centers with a functional TB diagnosis and treatment unit (including a functional laboratory), and in which no other programmatic or research projects were being undertaken, were eligible for inclusion. A total of 25 of 53 DHCs met these criteria. One center refused to participate, and the remaining 24 DHCs were stratified according to their estimated baseline sputum smear–positive detection rate, either less than or greater than or equal to 60 cases per 100 000 population, to account for variation in the recruitment of patients among DHCs. Within each stratum, 8 DHCs were randomly selected from the 12 and then allocated to the intervention or control groups using blocked randomization (FIGURE 1).

Participants, those administering the intervention, and those assessing outcomes were not masked to study group. All staff (TB control staff working at the DHCs and health posts [nurses, assistant nurses, and community health workers]) administering the intervention were trained in the intervention and therefore could not be masked to study group. In addition, TB nurses at the DHC were responsible for treatment and follow-up of patients, including collection of data for outcomes. Laboratory staff were not aware of to which group the DHCs were randomized. The ran-

Figure 1. Cluster Randomized Controlled Trial Flow Diagram



domization of DHCs to study groups only took place after all DHCs gave agreement to participate in the study.

Patients and Follow-up

The study population consisted of all individuals presenting to the DHC between June 2003 and May 2004, with newly diagnosed sputum smear–positive pulmonary TB (with at least 2 positive specimens), aged 15 years or older, and living in the district served by the DHC. Written informed consent was obtained at recruitment and patients were followed up during the course of their 8-month treatment regimen, with the last patients observed in January 2005. The study was approved by the ethics committee of the National Scientific Research Council of Senegal.

The TB nurses at the DHC were responsible for monitoring the recruitment, registration, treatment, and follow-up of patients. Formal monthly monitoring visits were conducted in both groups by specifically recruited field assistants, who supervised all activities and checked the completion of the forms. In both groups, following the procedures of the NTCP, patients were given appointments at the DHC at the end of months 2, 5, and 8 for clinical examination and collection of sputum samples. Decisions regarding the continuation of treatment were based on the result of the sputum smears.[11]

Analysis

The effect of the intervention was measured with the end result of treatment, using standard definitions set by the International Union Against Tuberculosis and Lung Diseases.[11] Primarily this was both the proportion of recruited patients experiencing treatment success (those patients cured and those completing their full course of treatment) and those defaulting from treatment. A *cured* patient was defined by a negative sputum smear at 8 months and on at least 1 previous occasion, while *completing treatment* were those patients missing smear results but who had finished their treatment regimen. A *defaulter* was defined as a patient who definitely stopped treatment before completion.

Analysis was based on intention to treat, conducted using methods described by Bennett et al[12] appropriate for a cluster randomized design with a small number of clusters, and undertaken using SAS version 8.02 with survival analysis conducted using STATA version 9.2 (StataCorp LP, College Station, Tex). The proportions of patients with each outcome were calculated for each cluster and the effect of the intervention was measured by the ratio (intervention group/control group) of the geometric means of these proportions, termed the unadjusted risk ratio (RR). An approximate variance of the cluster outcomes adjusted appropriately for stratification in the study design was the mean square error from an analysis of variance of the cluster outcomes including study group with 2 levels (intervention or control), baseline case notification rate strata with 2 levels (low or high), and their interaction. A 95% confidence interval (CI) for the RR used this approximate variance and a critical value from the *t* distribution with 12 *df*.

An adjusted analysis was also undertaken using the 2-stage approach,[12] replacing the cluster proportions with the ratio of the number of patients with each outcome over the cluster sum of expected values from a logistic regression model using patient-level data. The logistic regression model incorporated baseline measures for each outcome (the mean proportion of patients in 2000-2002, with each outcome categorized into 3 groups) and potentially important confounders (sex and age) as well as baseline case notification strata at 2 levels.

Secondary unsuccessful outcomes (ie, treatment failures [defined as a patient who remained or became smear positive at or after 5 months], transfers, and deaths) were rare events with at least 1 cluster experiencing no events. In these cases, the adjusted analysis was calculated as the risk difference, the difference between the observed and expected values.[13] The time to defaulting by treatment group was analyzed using Weibull regression, adjusting for age, sex, strata, and the baseline proportion of patients defaulting from treatment. The lack of independence among patients within the same DHC was accounted for with γ frailty. Time to default is illustrated using a Kaplan-Meier curve.

RESULTS

A total of 778 patients in the intervention group and 744 patients in the control group were enrolled and eligible for the study, ranging from 21 to 239 patients per DHC (TABLE 1). An additional 76 patients were found to be ineligible for the study as they lived outside the district.

At baseline, patient characteristics, such as age and sex, were distributed similarly between the intervention and control groups (Table 1). However, DHCs randomized to the intervention were closer to Dakar and had a higher percentage with a successful treatment outcome based on the mean for 2000-2002 than DHCs randomized to the control group.

Of those patients recruited and eligible, 1406 (92%) had a sputum smear at 2 months, 1261 (83%) at 5 months, and 1185 (78%) at 8 months. At all 3 occasions, a higher proportion of patients had a smear collected in the intervention group than in the control group (95% vs 90% at 2 months, 88% vs 77% at 5 months, and 84% vs 71% at 8 months, respectively).

Treatment outcomes are displayed in TABLE 2. Treatment was successful for 682 patients (87.7%) in the intervention group compared with 563 patients (75.7%) in the control group. The adjusted RR for treatment success was 1.18 (95% CI, 1.03-1.34). Adjusted RRs and risk differences for other treatment outcomes are reported in Table 2, adjusted for baseline measure, sex, age category, and baseline case notification strata. Distance from Dakar, severity of sputum, and patient's weight had little effect on the adjusted RRs for treatment success and default.

Treatment outcomes by cluster and study group are shown in TABLE 3. Two of the control clinics had more than 80% of their patients achieve successful outcomes while all of the intervention clinics achieved this level of success. Although there was a small number of deaths observed overall, 2 control clinics had high proportions of deaths. Adjusting for other variables had little effect on the adjusted RRs. The effect was consistent over intervention clusters as can be observed in Table 3.

Forty-three patients (5.5%) defaulted from treatment in the intervention group vs 125 patients (16.8%) in the control group (adjusted RR, 0.43; 95% CI, 0.21-0.89), suggesting that the risk of defaulting was nearly 60% lower in the intervention group. The intervention also significantly decreased the time to defaulting since the start of treatment (RR, 0.19; 95% CI, 0.07-0.49), adjusting for treatment group, age, sex, baseline case notification strata, and baseline proportion defaulting. This is illustrated in FIGURE 2, using a Kaplan-Meier curve.

Decentralization of care involved 42 health posts, with a median of 5 health posts per DHC. A median of 9 patients (range, 1-98 patients) used each health post. Of the 778 patients in the intervention group, 462 (59.4%) had their treatment supervised by a family member, 245 (31.5%) were supervised by a DHC nurse or health post nurse, and the remaining 71 (9.1%) were supervised by the com-

Table 1. Baseline Patient and District Health Center Characteristics*

Characteristics	Intervention (n = 778)	Control (n = 744)
Patient characteristics		
Age, y		
15-24	206 (26.5)	188 (25.3)
25-34	284 (36.5)	258 (34.7)
35-49	191 (24.6)	214 (28.8)
≥50	97 (12.5)	84 (11.3)
Male sex	512 (65.8)	502 (67.5)
Sputum smears (of the 3)		
At most 10-99 AFB in 100 fields	185 (23.8)	203 (27.3)
At most 1-10 AFB in ≥50 fields	255 (32.8)	239 (32.1)
At most >10 AFB in ≥20 fields	338 (43.4)	302 (40.6)
Weight, median (IQR), kg	52 (46-58)	51 (45-57)
District health center characteristics	(n = 8)	(n = 8)
No. of patients per health center, median (range)		
Detection rate <60 cases/100 000 population	84 (37-182)	36 (21-128)
Detection rate ≥60 cases/100 000 population	90 (25-186)	121 (41-239)
Distance from Dakar, median (IQR), km	75.5 (20.0-140.5)	196.5 (69.0-259.0)
Mean baseline treatment success of 2000-2002, median (IQR)	68.0 (57.5-69.6)	53.4 (40.9-63.8)
No. of centers with treatment success		
<50%	1	4
50%-68%	3	3
>68%	4	1

Abbreviations: AFB, acid-fast bacilli; IQR, interquartile range.
*Data are presented as number (percentage) unless otherwise specified. Because of rounding, percentages may not all total 100.

Table 2. Risk Ratios and Risk Differences for the Effect of the Intervention Group Relative to the Control Group

Treatment Outcome	Crude Risk Ratio (95% CI)	Adjusted Risk Ratio (95% CI)*	Adjusted Risk Difference (95% CI)†
Treatment success‡	1.25 (1.08 to 1.45)	1.18 (1.03 to 1.34)	
Cured	1.30 (1.10 to 1.54)	1.20 (1.05 to 1.37)	
Defaulted	0.25 (0.14 to 0.48)	0.43 (0.21 to 0.89)	
Transferred out			–0.6 (–4.3 to 3.2)
Treatment failure			1.6 (–1.2 to 4.5)
Death			–1.5 (–4.1 to 1.1)

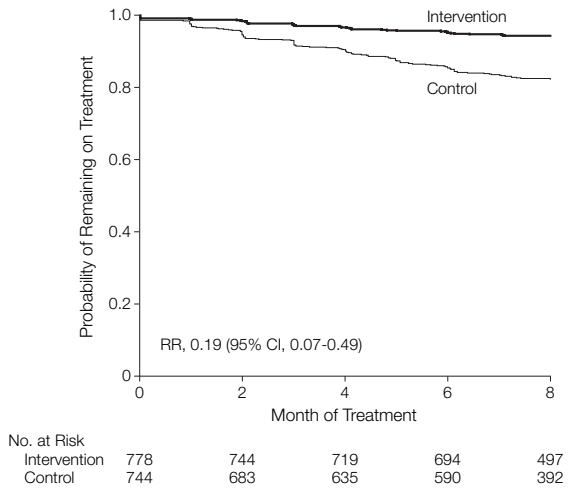
Abbreviation: CI, confidence interval.
*Adjusted for baseline measure, sex, age category, and baseline case notification strata. Distance from Dakar, severity of sputum, and patient's weight had little effect on the adjusted risk ratio.
†Given as a percentage. A negative risk difference implies that there was a reduction in the intervention group.
‡Treatment success is the sum of those patients cured and those who completed their 8-month course of treatment but were missing sputum smear test results.

Table 3. Treatment Outcomes by District Health Center

District Health Center	Total No. of Patients	Treatment Outcome, No. (%)						
		Treatment Success*	Cured	Completed Treatment	Defaulted	Transferred Out	Treatment Failure	Death
Intervention	778	682 (87.7)	649 (83.4)	33 (4.3)	43 (5.5)	29 (3.7)	12 (1.5)	12 (1.5)
1	182	153 (84.1)	136 (74.7)	17 (9.3)	14 (7.7)	5 (2.7)	7 (3.8)	3 (1.6)
2	59	54 (91.5)	53 (89.8)	1 (1.7)	2 (3.4)	2 (3.4)	0	1 (1.7)
3	109	103 (94.5)	103 (94.5)	0	3 (2.8)	2 (1.8)	1 (0.9)	0
4	37	32 (86.5)	32 (86.5)	0	1 (2.7)	1 (2.7)	1 (2.7)	2 (5.4)
5	186	153 (82.3)	145 (78.0)	8 (4.3)	15 (8.1)	14 (7.5)	1 (0.5)	3 (1.6)
6	39	36 (92.3)	34 (87.2)	2 (5.1)	1 (2.6)	1 (2.6)	0	1 (2.6)
7	25	21 (84.0)	20 (80.0)	1 (4.0)	2 (8.0)	0	2 (8.0)	0
8	141	130 (92.2)	126 (89.4)	4 (2.8)	5 (3.5)	4 (2.8)	0	2 (1.4)
Control	744	563 (75.7)	520 (69.9)	43 (5.8)	125 (16.8)	25 (3.4)	6 (0.8)	25 (3.4)
1	44	31 (70.5)	30 (68.2)	1 (2.3)	7 (15.9)	3 (6.8)	1 (2.3)	2 (4.5)
2	128	107 (83.6)	105 (82.0)	2 (1.6)	15 (11.7)	3 (2.3)	0	3 (2.3)
3	21	13 (61.9)	13 (61.9)	0	4 (19.0)	0	0	4 (19.0)
4	28	21 (75.0)	18 (64.3)	3 (10.7)	3 (10.7)	0	0	4 (14.3)
5	105	64 (61.0)	61 (58.1)	3 (2.9)	31 (29.5)	10 (9.5)	0	0
6	239	191 (79.9)	170 (71.1)	21 (8.8)	36 (15.1)	5 (2.1)	2 (0.8)	5 (2.1)
7	41	24 (58.5)	20 (48.8)	4 (9.8)	14 (34.1)	2 (4.9)	0	1 (2.4)
8	138	112 (81.2)	103 (74.6)	9 (6.5)	15 (10.9)	2 (1.4)	3 (2.2)	6 (4.3)

*Treatment success is the sum of those patients cured and those who completed their 8-month course of treatment but were missing sputum smear test results.

Figure 2. Kaplan-Meier Curve of the Time to Defaulting From Treatment by Study Group



RR indicates risk ratio; CI, confidence interval.

munity health worker or other community member. A higher percentage (88%) of patients (405/462) supervised by a family member were cured based on the results of sputum smears vs 77% of all other treatment supervisors (244/316). Additionally, 18 (3.9%) of 462 patients defaulted when treatment was supervised by family members compared with all other treatment supporters (25 [7.9%] of 316 patients). For the primary outcome of treatment success, the number needed to treat is 8.

COMMENT

The introduction of a comprehensive multitargeted intervention aimed at improving patient's adherence to treatment through improved counseling and communication between health staff and patients, decentralization of treatment involving community health workers, flexibility in the choice of DOT supporter, and reinforced supervision activities of remote health posts reduced the proportion of patients interrupting treatment before completion. This resulted in a higher proportion of successful treatment outcomes compared with the usual NTCP procedures, even after adjusting for the fact that the intervention DHCs were doing better at baseline. Also, we found that the choice of a DOT supporter among the patients' family members yielded better treatment outcomes than other DOT supporters.

A general improvement in the control group from baseline data was observed, suggesting that the initial training received and the monitoring of the health workers to ensure correct recording may have increased awareness among those workers and resulted in improved standards of care in this group. The reported RRs should therefore be considered as conservative and the intervention considered effective at improving adherence to treatment.

In the last 15 years, a variety of strategies aimed at improving treatment outcome have been tested around the world, including patients' incentives, tracing default patients, taking legal sanctions, and improving staff motivation or treatment supervision.[14,15] These interventions were generally targeted at a single element of control (eg, treatment delivery) and showed variable success. Of 3 RCTs conducted to compare self-administered with directly-observed therapy,[16-18] 2 trials showed that there was little to be gained by DOT only,[16,18] because approximately 30% of patients in these populations interrupted treatment before completion whatever the methods of treatment supervision. This opened the way to multitargeted approaches, a concept we used in this study, targeting together health staff, patients, and communities.[8,15]

Defaulting from treatment is one of the most important problems in TB control.[3,4] Studies performed in Madagascar[19] and in India[20] showed that the lack of information, poor communication with health staff, and lack of attention and support at the clinic were some of the many factors affecting patients' adherence to treatment. In our qualitative study, we found that the health staff can play a key role in achieving adherence to treatment, justifying the training component of the tested strategy and the need for improved counseling.[9]

Access to health care is the cornerstone of TB control programs that must ensure that patients receive a full course of treatment. In areas in which patients live far from health centers, the positive effect of free treatment is often offset by indirect transportation costs, and patients might prefer to give up treatment due to these costs.[5] The qualitative study suggested that access to drugs would be improved through decentralization of treatment.[9] Our findings are consistent with those reported from several countries in Africa,[21-23] in which decentralization was shown to be effective overall, although the magnitude of the effect on treatment outcome varied according to the country, the type of treatment, and the site identified for treatment delivery.

Directly observed therapy is central to the global strategy for effective TB control launched by the WHO in 1994 and named directly observed therapy, short course (DOTS).[24] In 2002, WHO recommended flexibility in implementing DOTS and promoted "a comprehensive and multifactorial approach."[25] Qualitative studies showed that patients who received the support and care of their families were more likely to adhere to therapy and achieve cure,[26] and newly patient-centered approaches were tested. Observational studies performed in Kenya, Malawi, and Uganda showed that the choice of DOT supporter by the patient, associated with the decentralization of treatment, improved treatment success rates.[21-23] Furthermore, a cluster RCT in South Africa reported improvements when lay health workers were involved in TB control,[27] although a study in Nepal[28] recently demonstrated that both family and community DOT supporters can achieve good treatment outcomes. Allowing a choice of treatment supporter provided the patients with the capacity to determine the mode of supervision that was the most appropriate to their daily life. In addition, this community-based approach made it possible for community health workers to trace default patients and bring them back to treatment.

Sustained supervision by the district health team is needed to ensure the continuity of this strategy through ensuring appropriate supply and safe storage of medication in distant places, and regular checks of recorded data. This intensified supervision certainly has a cost and requires appropriate managerial capacity but appears essential for improved TB control.

Because the intervention we tested was offered as a package, we cannot determine the effect of individual elements of the strategy. Some of these elements did not show conclusive results when tested elsewhere.[29] We believe, however, that coherent public health strategies are most often multitargeted, and strategies developed to improve adherence to treatment are likely to be complex[15]; hence, the development of comprehensive and multitargeted interventions.

We did not test study participants for human immunodeficiency virus as this was not routine practice in Senegal at the time of the study. The reported prevalence of human immunodeficiency virus infection in the general population in Senegal is 1.4%.[30]

To establish evidence-based recommendations, the RCT design has been proposed to test measures to promote adherence to treatment[31] in preference to observational studies, which have limited capacity to show the effect of introducing a new intervention. The effect of various single element strategies has been tested using the individual RCT design.[16-18] However, we chose the cluster RCT design to assess the effectiveness of our intervention, as other public health interventions based on strategies to promote adherence delivered in a standard way at the community level[27,28] have done. It was logistically easier to perform our intervention at the health center level, and the clustered design reduces contamination that could be problematic if the intervention was administered at the individual level.

The DHCs that participated in the study are generalizable to all DHCs in Senegal, representing centers in urban, semi-urban, or rural areas, and 7 of 11 administrative regions of Senegal. A total of 25 of 53 DHCs met the criteria to be included in the study. The 28 DHCs not included in the study were because of nonfunctional laboratories, the presence of another research study, a previous implementation of a decentralization process (supported by development aid organizations), no functional health posts, or unwillingness to perform the study.

Control of TB depends on effective treatment as well as effective strategies to support the process of care from detection of disease through the completion of appropriate treatment.[8] A key aspect of our approach was to identify, based on qualitative studies, an intervention that would be feasible, sustainable, and fully acceptable by the pa-

tients and the health care services.[31] This, we believe, is the path toward making TB control more responsive and reflective of local health systems and social constraints and resources. Our results show that the intervention we tested, consisting of a coherent package of sustainable activities targeting altogether health staff, patients, and communities, did improve treatment outcomes. This intervention could now be implemented in a stepwise manner throughout Senegal, and we believe that this approach may be generalized within the context of TB control programs in other resource-poor countries.

Author Contributions: Dr Lienhardt had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis. Drs Thiam and LeFevre contributed equally to the paper.
Study concept and design: Ndir, Lienhardt.
Acquisition of data: Thiam, Hane, Ndiaye, Ba, Ndir, Lienhardt.
Analysis and interpretation of data: Thiam, LeFevre, Fielding, Lienhardt.
Drafting of the manuscript: Thiam, LeFevre, Hane, Ba, Fielding, Ndir, Lienhardt.
Critical revision of the manuscript for important intellectual content: Thiam, LeFevre, Ndiaye, Fielding, Lienhardt.
Statistical analysis: LeFevre.
Obtained funding: Ndir, Lienhardt.
Administrative, technical, or material support: Thiam, Ndiaye, Ba, Ndir, Lienhardt.
Study supervision: Thiam, Hane, Ndiaye, Fielding, Lienhardt.
Financial Disclosures: None reported.
Funding/Support: This study was funded through a special program from the French Ministry of Research, called PAL+, which was granted in September 2000.
Role of the Sponsors: The sponsor of the study, the French based Institut de Recherche pour le Developpement (IRD), was involved at all stages of the study, which was conducted jointly and in close collaboration with the Senegalese National TB Control Program. Sponsor funds were provided to the authors in Dakar and to the Senegalese National TB Control Program. The sponsor helped in getting official contacts with the responsible persons at the Ministry of Health in Senegal and access to health centers involved in the study, and in collecting data throughout the study. The sponsor was informed on trial developments through regular visits and reports, and contributed to the preparation and review of the manuscript.
Acknowledgment: We thank all head physicians and staff in the concerned district health centers who contributed to the study. We also thank Laurent Vidal, PhD, Acteurs et Systèmes de santé en Afrique, IRD Université de Provence, Marseille, France, and Abdou Salam Fall, PhD, Institut Fondamental d'Afrique Noire (IFAN), Dakar, Senegal, for their contribution in the qualitative study that allowed the definition of the intervention; and Jessica A. Ogden, PhD, International Center for Research on Women, for her creative thinking and contribution to the development of the methods of the study. None received any compensation for their work.

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